

Fig. S1. Schematic representation of in vivo negative selection screen. Transposon site hybridization was used to find genes that were required for survival in vivo. The central principle to this approach is to inoculate animals with a transposon mutant library and to use microarray hybridization to find genes that are present in the initial inoculum, but lost in vivo. Each bacterium in the transposon mutant library contains a transposon interrupted gene. Pregnant guinea pigs were infected i.v. with the input library grown in BHI (input pool). Genes that are necessary for infection (gene A) or growth on BHI (gene C) have reduced fitness and become relatively absent under the respective growth conditions. Next, bacteria are isolated from maternal liver and placenta (output pools), mRNA is transcribed from the regions flanking the transposon, reverse transcribed to cDNA, and labeled with differential dyes. The dyed cDNAs are then mixed and hybridized to a microarray containing known oligos for all genes in the *L. monocytogenes* genome. Spots with a greater yellow signal from the input pool (gene A) suggest that the interrupted gene was relatively absent in vivo and thus important for infection. Spots with a greater blue signal from the output pool (gene C) suggest the interrupted gene is overabundant in vivo and is either more virulent in vivo or has a growth defect in BHI. Genes that are equally abundant (gene B) will have both dyes present on spots and suggest that they are not necessary for infection.

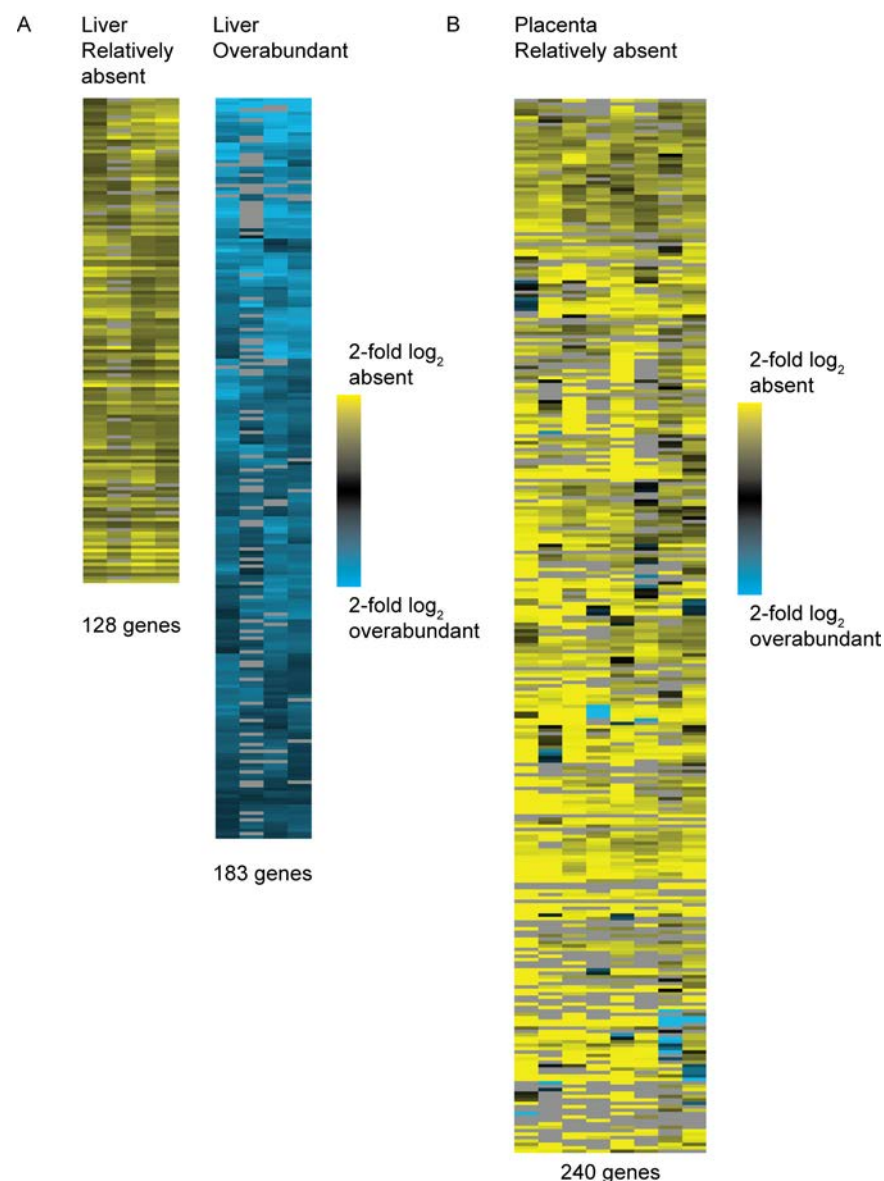


Fig. S2. Negative selection of *L. monocytogenes* mutants in vivo. Pregnant guinea pigs (n=4) were injected i.v. with 10^9 CFU of the transposon mutant library. Bacteria surviving 24 h.p.i in maternal liver (n=4) and placenta (n=8) were collected. 10^9 is the highest infectious dose we can use intravenously because we have observed sudden death of the guinea pigs shortly after i.v. inoculation with higher doses. With 10^9 CFU i.v. the animals will die between 24 and 48 h.p.i. Since know that placental colonization is relatively restricted, and that we could not increase the dose or sacrifice the animals at later time points we used the 8 placentas with the highest bacterial burden from 3 independent animal infections. The transposon mutants present in each organ sample versus BHI were identified by microarray analysis. Yellow represents relative absence of signal in the organ compared with BHI, and blue represents overabundance of signal in the organ relative to BHI. Heat maps of genes with relative absence or overabundance in liver versus BHI (A), and placenta versus BHI (B).

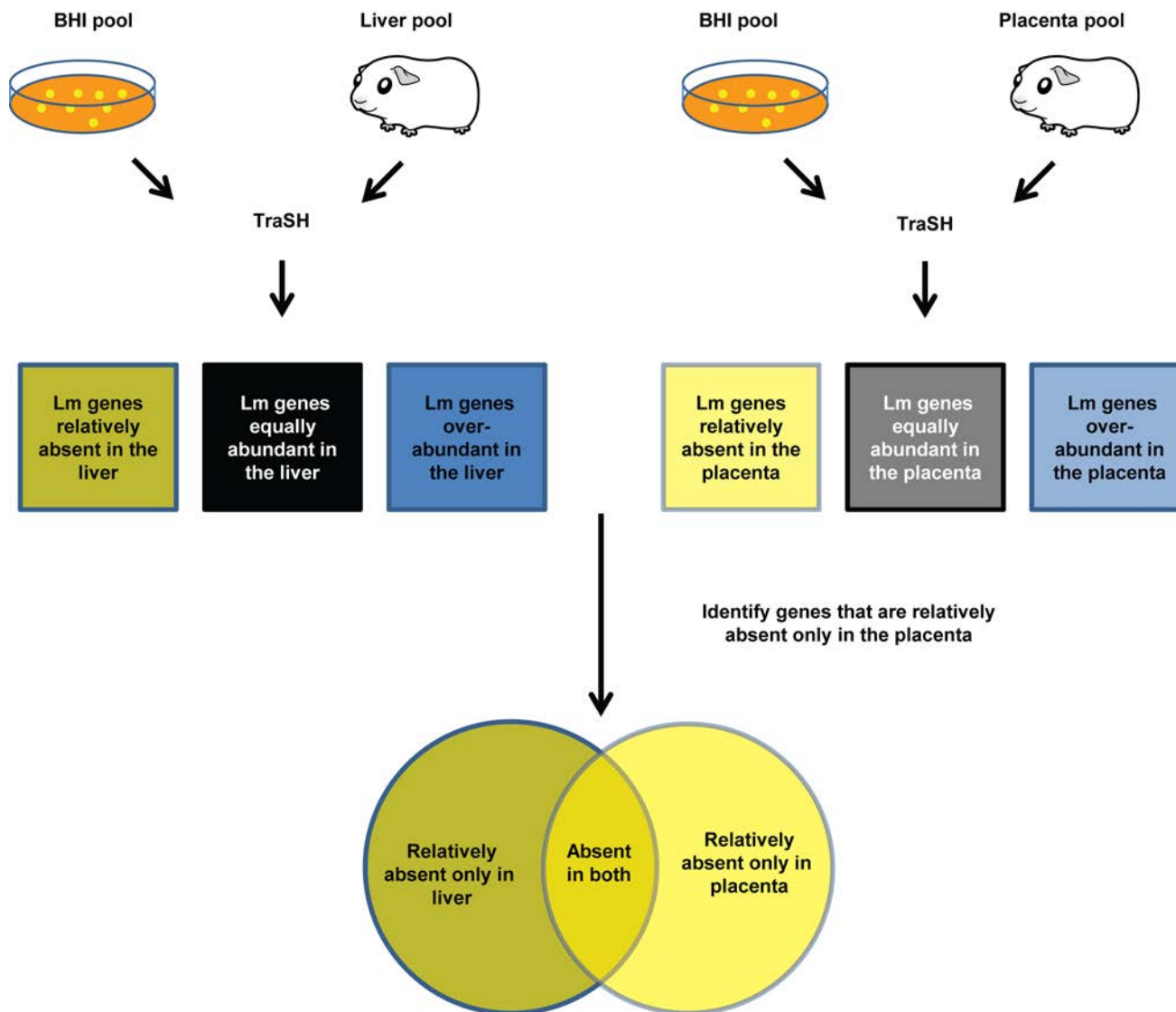


Fig. S3. Schematic representation of analysis performed to identify genes specifically relevant for placental infection. Negative selection screen was used to identify genes that were relatively absent in the placenta but present or overabundant in the liver. *L. monocytogenes* was isolated from liver and placenta, then compared to the input library plated on BHI to determine genes that were relatively absent (yellow), equally abundant (black) or overabundant (blue) relative to BHI. Relatively absent genes were then compared between the liver pool and the placenta pool and genes were selected that were only absent in the placenta.

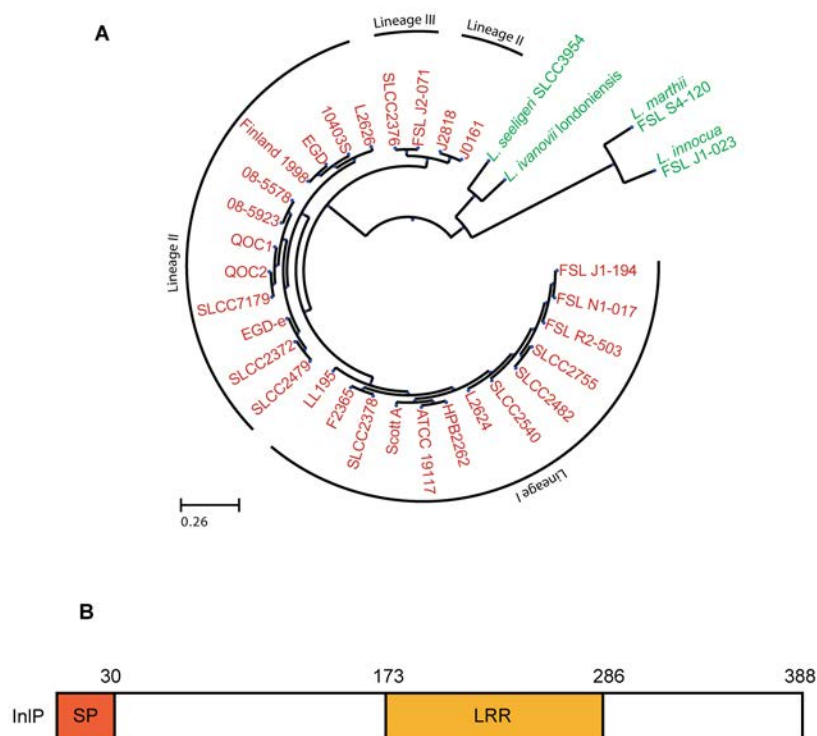


Fig. S4. InIP is conserved in the human pathogen *L. monocytogenes*. (A) Neighbor joined phylogram representing the distances between amino acid sequences extracted from complete and annotated *Listeria* spp. genomes. Strains in red indicate that the given *L. monocytogenes* genome contained a sequence with extremely high local-alignment with the InIP protein; *i.e.* there is a homolog in that strain with at least 90% identity on 100% of the query. Non-pathogenic *Listeria* species are in green. Scale bar represents average amino acid changes per site. (B) Diagram of InIP with predicted domains (SP=signal peptide, LRR=leucine-rich repeat). Domains were predicted by SMART. Numbers refer to amino acid position.

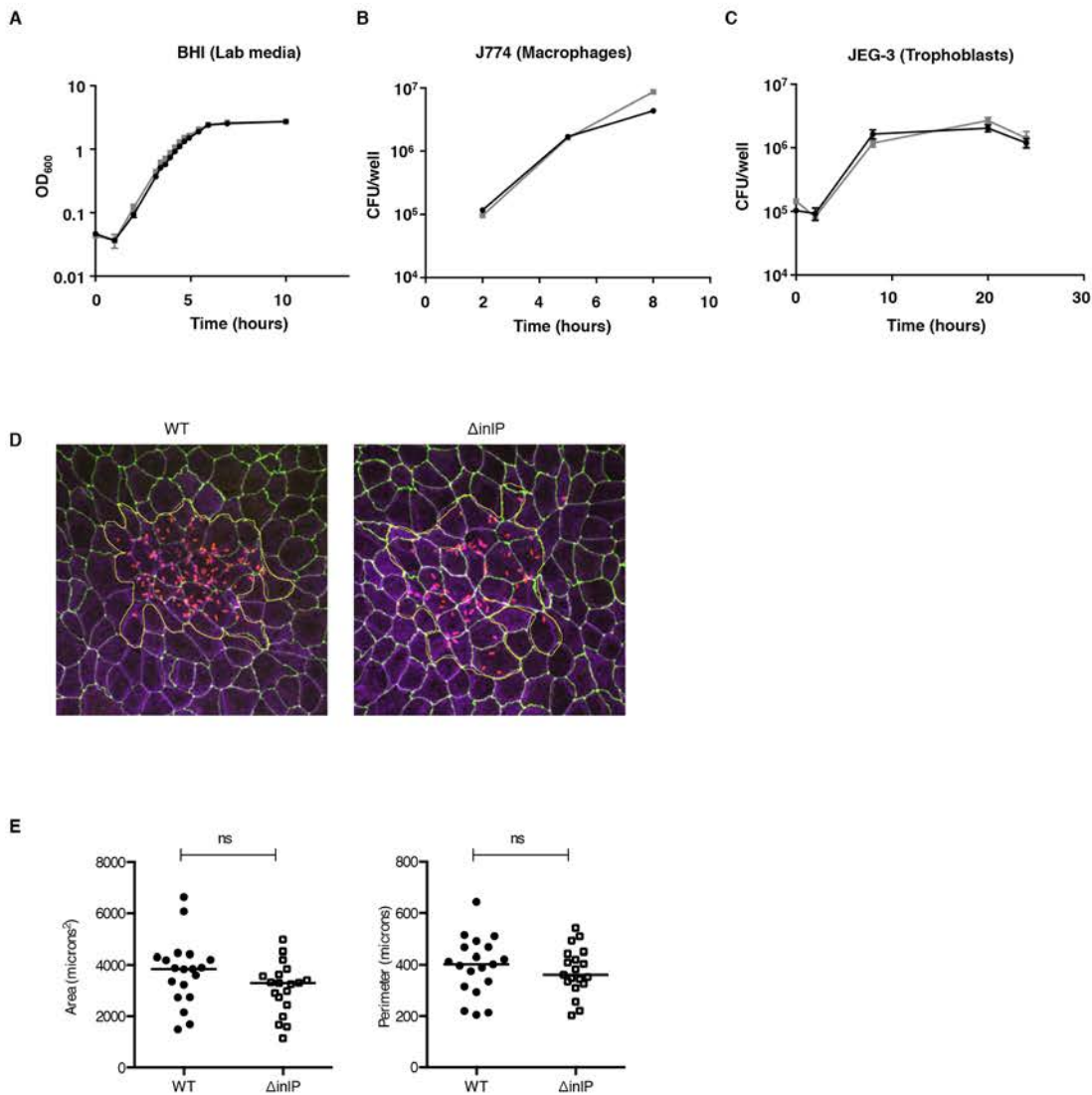


Fig. S5. Growth curves and cell-to-cell spread of wild type and $\Delta iniP$ under different in vitro conditions. For growth curves wild type and $\Delta iniP$ and represented by black and gray lines, respectively. (A) Extracellular growth in BHI broth at 37°C (average of two independent experiments performed in triplicate). Intracellular growth by gentamicin protection assay in (B) J774: murine macrophage-like cell line (one of two representative experiments), (C) JEG-3: human choriocarcinoma cell line (average of five independent experiments performed in triplicate). Error bars: SEM. (D) Representative Maximum Intensity Z-projection image of polarized Madin-Darby Canine Kidney (MDCK) cells 8 hours after infection with either WT (filled circles) or $\Delta iniP$ (empty squares) stained for *L. monocytogenes* (red), ZO-1 (green), and actin (purple). Yellow line highlights outer edge of infectious focus. (E) Quantification of the size (area and perimeter) of infectious foci (n=19 foci for each strain, from 2 independent experiments). Bar: Median.

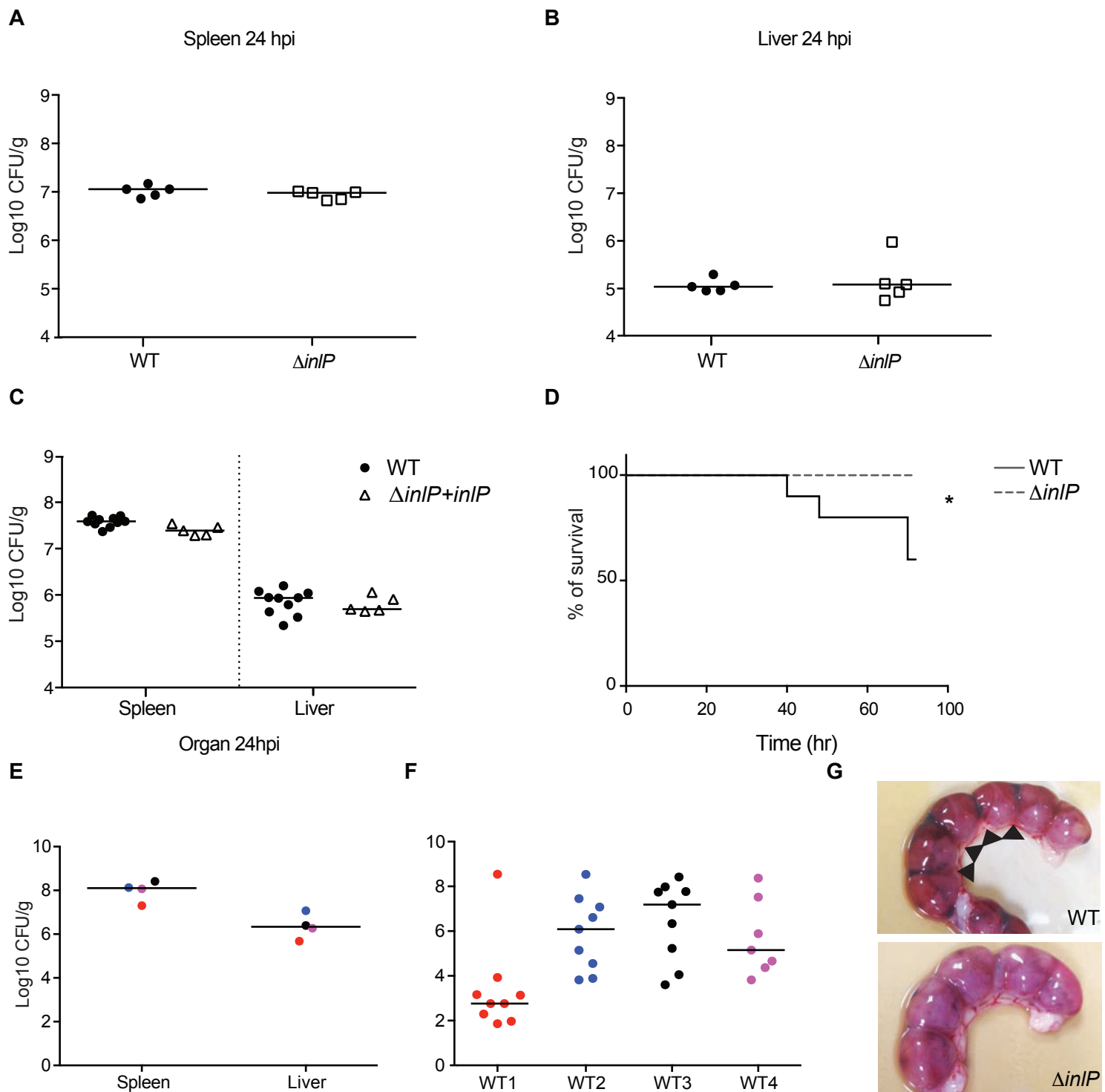


Fig. S6. InIP is a virulence determinant in mice. CFU in (A) spleen and (B) liver 24 h.p.i. of non-pregnant mice with 10^4 CFU of wild type (WT) or $\Delta inIP$. (C) Non-pregnant mice were infected i.v. with 7×10^4 CFU of WT or $\Delta inIP$ complemented with *inIP* ($\Delta inIP+inIP$). CFU/gram were enumerated in spleen and liver at 24 h.p.i. (D) Kaplan-Meier survival curve of non-pregnant mice infected with 7×10^4 CFU of wild type (black line) versus $\Delta inIP$ (dashed gray line). Statistical analysis: Log-rank (Mantel-cox) test for Kaplan-Meier survival curve: $*=P<0.05$. (E-F) Bacterial burden in four randomly chosen wild type infected mice that are included in Fig. 2D-F. Organs from each mouse are color-coded to show variability in placental CFU in each animal. (G) Gravida uteri 48 h.p.i. with 10^4 CFU on day 10.5 of gestation. WT but not $\Delta inIP$ infected feto-placental units, showed widespread hemorrhages (arrowheads).

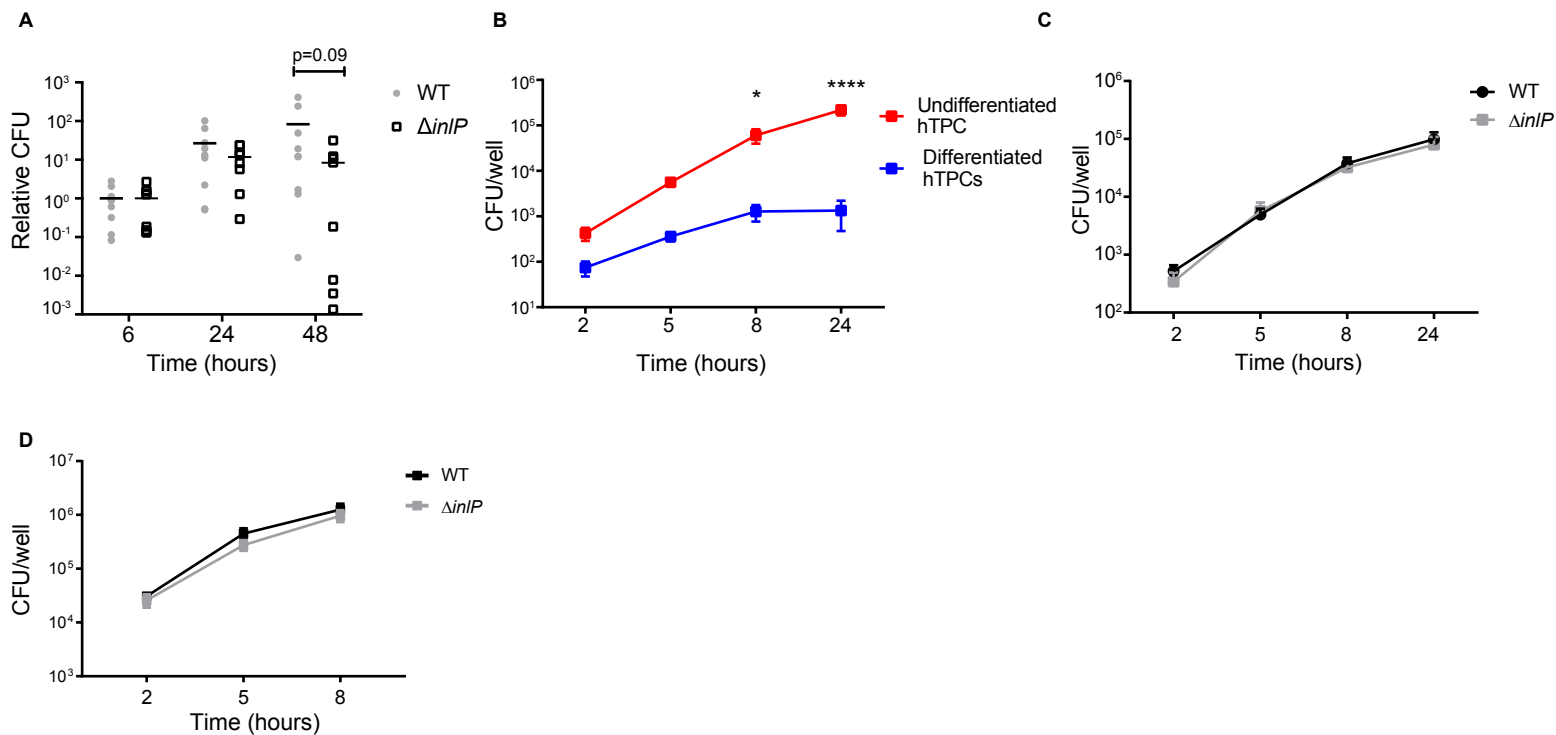


Fig. S7. Infection of primary human decidual organ cultures, human trophoblast progenitor cells (hTPC), and primary murine mixed glial cell cultures. (A) Primary human decidual organ cultures from 3 donors (at least 3 cultures per donor at each time point) were infected with wild type (WT, grey circles) or $\Delta inIP$ (empty squares) for 6, 24, or 48 hours. Bacterial burden was normalized to 6 h.p.i. for each donor (relative CFU). Mann-Whitney U test was used for statistical analysis: $P=0.09$. Horizontal bars: median. (B) Comparison of WT intracellular growth curve in differentiated (blue) and undifferentiated (red) hTPCs. Symbols represent the average of multiple independent experiments (differentiated $N = 4$, undifferentiated $N=3$). Error bars represent SEM. Two way ANOVA with Sidak's multiple comparison test was used for statistical analysis: * $P < 0.05$, **** $P < 0.0001$. (C) Undifferentiated hTPCs were infected with either WT (black) or $\Delta inIP$ (gray). (D) Murine mixed glial cells infected with either WT or $\Delta inIP$. Error bars represent SEM. Symbols represent the average of at least two independent experiments performed in triplicate. Statistical analysis using a two-way ANOVA found no significant differences in intracellular growth between the two strains.

Supplementary Table 1. Genes absent in the liver vs BHI

Locus	Gene	TIGR annotation
lmo0017		similar to Bacillus anthracis CapA protein (polyglutamate capsule biosynthesis)
lmo0018		beta-glucosidase
lmo0031		transcriptional regulator LacI family
lmo0033		similar to endoglucanase
lmo0037		similar to amino acid transporter
lmo0038		conserved hypothetical protein
lmo0105		highly similar to chitinase B
lmo0124		unknown
lmo0171		similar to internalin proteins, putative peptidoglycan bound protein (LPXTG motif)
lmo0174		similar to transposase
lmo0201	plcA	phosphatidylinositol-specific phospholipase c
lmo0202	hly	listeriolysin O precursor
lmo0203	mpl	zinc metallopeptidase
lmo0262	inlG	internalin G
lmo0271		highly similar to phospho-beta-glucosidase
lmo0327		leucine rich repeat domain/ LPXTG-motif cell wall anchor domain protein
lmo0331		immunoreactive 47 kDa antigen PG97
lmo0332		lacitehtopyh
lmo0333		similar to internalin proteins, putative peptidoglycan bound protein (LPXTG motif)
lmo0334		unknown
lmo0335		conserved hypothetical protein
lmo0348		similar to dihydroxyacetone kinase
lmo0356		oxidoreductase, YhhX family
lmo0357		similar to PTS system, enzyme IIA component
lmo0367		Tat-translocated enzyme
lmo0409		similar to internalin, peptidoglycan bound protein (LPxTG motif)
lmo0416		similar to putative transcription regulator
lmo0419		similar to unknown protein
lmo0431		similar to acetyltransferase
lmo0432		similar to oxidoreductase
lmo0447		similar to glutamate decarboxylase
lmo0448		similar to amino acid antiporter
lmo0450		similar to unknown proteins
lmo0451		conserved hypothetical protein
lmo0452		peptidase, putative
lmo0455		conserved hypothetical protein
lmo0457		similar to unknown proteins
lmo0476		similar to oxetanocin A resistance protein oxrB
lmo0479		putative secreted protein
lmo0480		similar to putative transcriptional regulator
lmo0489		similar to NADH:flavin oxidoreductase
lmo0490		similar to shikimate 5-dehydrogenase
lmo0492		similar to transcriptional regulator (LysR family)
lmo0507		similar to PTS system, Galactitol-specific IIB component
lmo0581		conserved hypothetical protein

lmo0588		similar to DNA photolyase
lmo0616		C-terminal domain similar to glycerophosphoryl diester phosphodiesterase
lmo0627		peptidoglycan bound protein (LPXTG motif) similar to adhesin
lmo0628		unknown
lmo0633		similar to PTS system, fructose-specific IIB component
lmo0634		similar to an E. coli putative tagatose 6-phosphate kinase
lmo0740		similar to putative transcription regulator
lmo0743		unknown
lmo0744		similar to ABC transporter, ATP-binding protein
lmo0746		hypothetical
lmo0752		weakly similar to a putative haloacetate dehalogenase
lmo0754		weakly similar to a bile acid 7-alpha dehydratase
lmo0801		similar to internalin, putative peptidoglycan bound protein (LPXTG motif)
lmo0831		unknown
lmo0832		similar to transposase
lmo0833		similar to transcriptional regulator
lmo0834		conserved hypothetical protein
lmo0835		putative peptidoglycan bound protein (LPXTG motif)
lmo0837		ABC transporter, ATP-binding protein
lmo0971	DltD	D-alanine esterification of lipoteichoic acid and wall teichoic acid
lmo0980		ABC transporter, permease protein
lmo1019		similar to B. subtilis YitL protein
lmo1134		transcriptional regulator, MerR family
lmo1155		similar to diol dehydrase (diol dehydratase) gamma subunit (pddC)
lmo1175	eutB	similar to ethanolamine ammonia-lyase, heavy chain
lmo1186		similar to ethanolamine utilization protein EutH - Escherichia coli
lmo1187		similar to ethanolamine utilization protein EutQ
lmo1235		similar to aspartokinase II alpha subunit
lmo1255		PTS system, trehalose-specific, IIBC component
lmo1256		unknown
lmo1258		unknown
lmo1505		similar to ABC transporter, ATP-binding protein
lmo1506		ABC transporter, permease protein
lmo1507		similar to two-component response regulators
lmo1508		similar to two-component sensor histidine kinase
lmo1586		similar to unknown proteins
lmo1622		similar to unknown proteins
lmo1646		similar to putative exonucleases SbcD
lmo1651		ABC transporter, ATP-binding protein
lmo1740		amino acid ABC transporter, permease protein
lmo1765	purH	phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase
lmo1766	purN	phosphoribosylglycinamide formyltransferase
lmo1768	purF	amidophosphoribosyltransferase
lmo1769		phosphoribosylformylglycinamide synthase II
lmo1772	purC	phosphoribosylaminoimidazole succinocarboxamide synthetase
lmo1774	purK	phosphoribosylaminoimidazole carboxylase II
lmo1789		weakly similar to Nad(P)h Oxidoreductase chain B

lmo1798		similar to unknown protein
lmo1799		cell wall surface anchor family protein, authentic frameshift
lmo1822		similar to RNA-binding Sun protein
lmo1990	leuD	hypothetical protein
lmo1998		similar to opine catabolism protein
lmo2002		similar to PTS mannose-specific enzyme IIB component
lmo2003		transcriptional regulator, GntR family
lmo2004		similar to transcription regulator GntR family
lmo2135		similar to PTS system, fructose-specific enzyme IIC component
lmo2143		weakly similar to mannose-6-phosphate isomerase
lmo2286	gp17	holin-like protein, putative
lmo2288		Protein gp15 [Bacteriophage A118]
lmo02333		competence transcription factor ComK, interruption-C
lmo2363		glutamate decarboxylase beta
lmo2434		highly similar to glutamate decarboxylases
lmo2444		similar to glycosidase
lmo2445		similar to internalin
lmo2474		conserved hypothetical protein
lmo2497		phosphate ABC transporter, permease protein
lmo2498		similar to phosphate ABC transporter (permease protein)
lmo2602		conserved hypothetical protein
lmo2648		similar to Phosphotriesterase
lmo2661		similar to ribulose-5-phosphate 3-epimerase
lmo2682		potassium-transporting ATPase, A subunit
lmo2734		glycosyl hydrolase, family 38
lmo2781		beta-glucosidase
lmo2785	kat	catalase
lmo2815		similar to reductases
lmo2816		similar to transport protein
lmo2817		carboxypeptidase, putative
lmo2818		similar to transmembrane efflux protein
lmo2836		alcohol dehydrogenase, zinc-dependent
lmo2837		similar to sugar ABC transporter permease protein
lmo2838		similar to sugar ABC transporter permease protein
lmo2848		highly similar to L-rhamnose isomerase
lmo2849		rhamnulokinase

Supplementary Table 1. Genes absent in placenta vs BHI

Locus	Gene	TIGR annotation
intergenic between comFA and lmo2514		hypothetical protein
intergenic between lmo2046 and rpmF		hypothetical protein
intergenic between lmo2566 and lmo2567		hypothetical protein
lmo0009		similar to spermidine N1-acetyltransferase
lmo0014	qoxB	quinol oxidase AA3, subunit I
lmo0016	qoxD	highly similar to quinol oxidase aa3-600 chain IV
lmo0018		beta-glucosidase
lmo0019		unknown
lmo0020		similar to transcriptional regulator (GntR family)
lmo0031		transcriptional regulator LacI family
lmo0037		similar to amino acid transporter
lmo0044	rpsF	ribosomal protein S6
lmo0051		similar to 2-components response regulator protein (AgrA from Staphylococcus)
lmo0084		similar to oxidoreductases
lmo0085		unknown
lmo0101		transcriptional regulator, ArsR family
lmo0102		unknown
lmo0106		similar to transcription regulator
lmo0112		weakly similar to transcription regulators, Fnr/Crp family
lmo0171		similar to internalin proteins, putative peptidoglycan bound protein (LPXTG motif)
lmo0201	plcA	phosphatidylinositol-specific phospholipase c
lmo0203	mpl	zinc metalloproteinase
lmo0208		conserved hypothetical protein
lmo0209		unknown
lmo0221		conserved hypothetical protein
lmo0222		conserved hypothetical protein
lmo0223	cysK	highly similar to cysteine synthase
lmo0224	sul	highly similar to dihydropteroate synthases
lmo0227		dihydrouridine synthase family protein
lmo0240		conserved hypothetical protein
lmo0243		RNA polymerase sigma-30 factor
lmo0246	nusG	transcription antitermination factor
lmo0263	inlH	internalin H
lmo0267		similar to other proteins
lmo0268		phosphoglycerate mutase family protein
lmo0269		transporter homolog lmo0269 [imported]
lmo0271		highly similar to phospho-beta-glucosidase
lmo0273		unknown
lmo0274		unknown
lmo0281		conserved hypothetical protein
lmo0292		similar to heat-shock protein htrA serine protease
lmo0348		similar to dihydroxyacetone kinase
lmo0356		oxidoreductase, YhhX family
lmo0367		Tat-translocated enzyme
lmo0369		conserved hypothetical protein TIGR01033
lmo0371		similar to transcription regulator (GntR family)
lmo0372		glycosyl hydrolase, family 1
lmo0386		similar to B. subtilis lmoD protein, to acetolactate synthase
lmo0396		similar to 1-pyrroline-5-carboxylate reductase (ProC)
lmo0405		phosphate transporter family protein
lmo0409		similar to internalin, peptidoglycan bound protein (LPxTG motif)

lmo0412		conserved hypothetical protein
lmo0416		similar to putative transcription regulator
lmo0452		peptidase, putative
lmo0457		similar to unknown proteins
lmo0476		HD domain protein
lmo0477		conserved hypothetical protein
lmo0479		putative secreted protein
lmo0480		similar to putative transcriptional regulator
lmo0492		similar to transcriptional regulator (LysR family)
lmo0508		PTS system, galactitol-specific, IIC component, putative
lmo0511		conserved hypothetical protein
lmo0516		similar to <i>Bacillus anthracis</i> encapsulation protein CapA
lmo0518		membrane protein, putative
lmo0539		tagatose 1,6-diphosphate aldolase, putative
lmo0582	iap	P60 extracellular protein, invasion associated protein Iap
lmo0583		similar to preprotein translocase SecA subunit
lmo0594		similar to homoserine O-acetyltransferase
lmo0604		similar to <i>B. subtilis</i> YvIA protein
lmo0605		membrane protein, putative
lmo0606		similar to transcription regulator MarR family
lmo0607		similar to ABC transporter, ATP-binding protein
lmo0608		similar to ABC transporter, ATP-binding protein
lmo0610		similar to internalin proteins, putative peptidoglycan bound protein (LPXTG motif)
lmo0611		similar to acyl-carrier protein phosphodiesterase and NAD(P)H dehydrogenase
lmo0613		similar to oxidoreductase
lmo0621		membrane protein, putative
lmo0625		unknown
lmo0627		peptidoglycan bound protein (LPXTG motif) similar to adhesin
lmo0636		Rrf2 family protein
lmo0647		unknown
lmo0653		unknown
lmo0673		unknown
lmo0676		similar to flagellar biosynthetic protein FliP
lmo0677		similar to flagellar biosynthesis protein FliQ
lmo0678		similar to flagellar biosynthetic protein FliR
lmo0693	fliY	flagellar motor switch domain protein
lmo0785		similar to transcriptional regulator (NifA/NtrC family)
lmo0789		similar to conserved hypothetical proteins
lmo0790		similar to transcription regulator (EbsC from <i>Enterococcus faecalis</i>)
lmo0799		unknown
lmo0801		similar to internalin, putative peptidoglycan bound protein (LPXTG motif)
lmo0810		spermidine/putrescine ABC transporter, spermidine/putrescine-binding protein
lmo0811		carbonic anhydrase
lmo0833		similar to transcriptional regulator
lmo0834		conserved hypothetical protein
lmo0836		similar to <i>B. subtilis</i> YrkR protein
lmo0837		ABC transporter, ATP-binding protein
lmo0843		similar to <i>B. subtilis</i> protein YsdA
lmo0867		unknown
lmo0881		unknown
lmo0882		similar to <i>B. subtilis</i> YdbS protein
lmo0908		similar to membrane proteins
lmo0910		membrane protein, putative

lmo0935		similar to B. subtilis CspR protein, rRNA methylase homolog
lmo0936		similar to Nitroflavin-reductase
lmo0937		unknown
lmo0943	fri	non-heme iron-binding ferritin
lmo0945		similar to C-terminal part of B. subtilis ComEC protein and to ComEA
lmo0950		unknown
lmo0957		glucosamine-6-phosphate isomerase
lmo0971	dltD	hypothetical protein
lmo0992		conserved hypothetical protein
lmo0993		cation transport protein
lmo1028		similar to B. subtilis YkzG protein
lmo1059		unknown
lmo1219		unknown
lmo1220		similar to unknown protein
lmo1221	pheS	phenylalanyl-tRNA synthetase alpha subunit
lmo1255		PTS system, trehalose-specific, IIBC component
lmo1256		unknown
lmo1257		unknown
lmo1258		unknown
lmo1260	proB	gamma-glutamyl kinase
lmo1267	tig	trigger factor (prolyl isomerase)
lmo1333		similar to B. subtilis YqzC protein
lmo1334		similar to B. subtilis YqzD protein
lmo1337		similar to B. subtilis yqgP
lmo1366		conserved hypothetical protein
lmo1368	recN	DNA repair and genetic recombination
lmo1389		similar to sugar ABC transporter, ATP-binding protein
lmo1394		similar to 3-ketoacyl-acyl carrier protein reductase
lmo1405		similar to putative anti-terminator regulatory protein
lmo1406	pflB	pyruvate formate-lyase
lmo1493		similar to oligopeptidase
lmo1494		similar to 5-methylthioadenosine/S-adenosylhomocysteine nucleosidase
lmo1495		similar to unknown proteins
lmo1505		similar to ABC transporter, ATP-binding protein
lmo1506		ABC transporter, permease protein
lmo1507		similar to two-component response regulators
lmo1509		similar to exodeoxyribonuclease V
lmo1510		similar to unknown proteins
lmo1539		glycerol uptake facilitator protein
lmo1586		similar to unknown proteins
lmo1595		similar to unknown protein
lmo1603		aminopeptidase, putative
lmo1609		thioredoxin family protein
lmo1625		polysaccharide biosynthesis family protein
lmo1683		similar to transcription regulators (Fur family), PerR in B. subtilis
lmo1685	gsaB	glutamate-1-semialdehyde-2,1-aminomutase 2
lmo1687		similar to hypothetical proteins
lmo1697		cation efflux family protein
lmo1703		RNA methyltransferase, TrmA family
lmo1705		deoxynucleoside kinase family protein
lmo1736		similar to unknown proteins
lmo1737		alcohol dehydrogenase, iron-dependent
lmo1740		amino acid ABC transporter, permease protein

lmo1741		similar to two-component sensor histidine kinase
lmo1742	adeC	highly similar to adenine deaminases
lmo1743		unknown
lmo1762		conserved hypothetical protein
lmo1765	purH	phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase
lmo1766	purN	phosphoribosylglycinamide formyltransferase
lmo1781		unknown
lmo1799		cell wall surface anchor family protein, authentic frameshift
lmo1849		manganese ABC transporter, ATP-binding protein
lmo1850		similar to transcriptional regulator (MarR family)
lmo1851		similar to carboxy-terminal processing proteinase
lmo1860		similar to peptidyl methionine sulfoxide reductases
lmo1861		conserved hypothetical protein
lmo1864		hemolysin III
lmo1865		similar to conserved hypothetical proteins
lmo1877		formate--tetrahydrofolate ligase
lmo1881		5'-3' exonuclease family protein
lmo1918		bacteriochlorophyll synthase, 43 kDa subunit
lmo1940		similar to asparaginase
lmo1973		similar to PTS system enzyme II A component
lmo1974		similar to transcription regulators, (GntR family)
lmo1980		unknown
lmo1992		similar to alpha-acetolactate decarboxylase
lmo2004		similar to transcription regulator GntR family
lmo2050		daunorubicin resistance protein
lmo2054		conserved hypothetical protein
lmo2055		similar to unknown proteins
lmo2056		similar to unknown proteins
lmo2057	ctaB	protoheme IX farnesyltransferase
lmo2058	ctaA	similar to heme O oxygenase
lmo2059		similar to potassium channel subunit
lmo2079		unknown
lmo2086		weakly similar to transcription regulators
lmo2105		similar to ferrous iron transport protein B
lmo2107		transcriptional regulator, DeoR family
lmo2143		weakly similar to mannose-6-phosphate isomerase
lmo2148		similar to unknown proteins
lmo2157	sepA	sepA
lmo2187		unknown
lmo2203		N-acetylmuramoyl-L-alanine amidase, family 4
lmo2207		membrane protein, putative
lmo2208		similar to unknown protein
lmo2216		similar to histidine triad (HIT) protein
lmo2238		similar to transport system permease protein
lmo2239		unknown
lmo2240		similar to ABC transporter (ATP-binding protein)
lmo2242		similar to O6-methylguanine-DNA methyltransferase
lmo2243		similar to methylphosphotriester-DNA alkyltransferase and transcriptional regulator
lmo2244		similar to putative ribosomal large subunit pseudouridine synthase
lmo2246		similar to unknown proteins
lmo2264		similar to unknown proteins
lmo2286	gp17	holin-like protein, putative
lmo2288		Protein gp15 [Bacteriophage A118]

lmo2362		similar to amino acid antiporter (acid resistance)
lmo2408		similar to repressor protein
lmo2419		similar to ABC transporter (ATP-binding protein)
lmo2430		iron compound ABC transporter, permease protein
lmo2433		similar to acetyltransferase
lmo2439		unknown
lmo2444		similar to glycosidase
lmo2451		similar to preprotein translocase subunit SecG
lmo2452		similar to carboxylesterase
lmo2469		similar to amino acid transporter
lmo2470		similar to internalin proteins
lmo2471		similar to NADH oxidase
lmo2474		conserved hypothetical protein
lmo2490		similar to B. subtilis CsbA protein
lmo2547		homoserine dehydrogenase
lmo2552	murZ	UDP-N-acetylglucosamine 1-carboxyvinyltransferase
lmo2567		conserved hypothetical protein
lmo2637		lipoprotein, putative
lmo2638		pyridine nucleotide-disulfide oxidoreductase family protein
lmo2657		deoxyguanosinetriphosphate triphosphohydrolase
lmo2705		conserved hypothetical protein
lmo2733		PTS system, fructose-specific, IIABC component
lmo2751		ABC transporter, ATP-binding/permease protein
lmo2766		phosphosugar-binding transcriptional regulator, RpiR family
lmo2817		carboxypeptidase, putative
lmo2842		transcriptional regulator, LacI family
lmo2849		rhamnulokinase
lmos10	LhrC-4	miscRNA
lmos27	rli33	miscRNA
lmos50	rli42	miscRNA

Supplementary Table 1. Genes absent in placenta vs liver

Locus	Gene	TIGR annotation
intergenic between comFA and lmo2514		lipoprotein, putative
intergenic between lmo2046 and rpmF		hypothetical protein
intergenic between lmo2566 and lmo2567		hypothetical protein
lmo0014	qoxB	AA3-600 quinol oxidase subunit I
lmo0016	qoxD	highly similar to quinol oxidase aa3-600 chain IV
lmo0019		unknown
lmo0020		similar to transcriptional regulator (GntR family)
lmo0044	rpsF	ribosomal protein S6
lmo0051		similar to 2-components response regulator protein (AgrA from Staphylococcus)
lmo0084		similar to oxidoreductases
lmo0085		unknown
lmo0101		transcriptional regulator, ArsR family
lmo0102		unknown
lmo0106		similar to transcription regulator
lmo0112		weakly similar to transcription regulators, Fnr/Crp family
lmo0208		conserved hypothetical protein
lmo0209		unknown
lmo0221		conserved hypothetical protein
lmo0222		conserved hypothetical protein
lmo0223	cysK	cysteine synthase A
lmo0224	sul	highly similar to dihydropteroate synthases
lmo0227		dihydrouridine synthase family protein
lmo0240		transporter homolog lmo0269 [imported]
lmo0240		conserved hypothetical protein
lmo0243		RNA polymerase sigma-30 factor
lmo0246	nusG	transcription antitermination factor
lmo0263	inlH	internalin H
lmo0267		similar to other proteins
lmo0268		phosphoglycerate mutase family protein
lmo0269		transporter, putative
lmo0273		unknown
lmo0274		unknown
lmo0281		conserved hypothetical protein
lmo0292		similar to heat-shock protein htrA serine protease
lmo0367		conserved hypothetical protein similar to B. subtilis YwbN protein
lmo0369		conserved hypothetical protein TIGR01033
lmo0371		similar to transcription regulator (GntR family)
lmo0372		glycosyl hydrolase, family 1
lmo0386		similar to B. subtilis IolD protein, to acetolactate synthase
lmo0396		similar to 1-pyrroline-5-carboxylate reductase (ProC)
lmo0412		conserved hypothetical protein
lmo0476		HD domain protein
lmo0477		conserved hypothetical protein
lmo0508		PTS system, galactitol-specific, IIC component, putative
lmo0511		conserved hypothetical protein
lmo0516		similar to Bacillus anthracis encapsulation protein CapA
lmo0518		membrane protein, putative
lmo0582	iap	protein P60
lmo0583		similar to preprotein translocase SecA subunit
lmo0594		similar to homoserine O-acetyltransferase
lmo0604		similar to B. subtilis YvIA protein
lmo0605		membrane protein, putative
lmo0606		similar to transcription regulator MarR family

lmo0607		similar to ABC transporter, ATP-binding protein
lmo0608		ABC transporter, ATP-binding/permease protein
lmo0610		similar to internalin proteins, putative peptidoglycan bound protein (LPXTG motif)
lmo0611		similar to acyl-carrier protein phosphodiesterase and NAD(P)H dehydrogenase
lmo0613		similar to oxidoreductase
lmo0621		membrane protein, putative
lmo0625		unknown
lmo0636		Rrf2 family protein
lmo0647		unknown
lmo0653		unknown
lmo0673		unknown
lmo0676		similar to flagellar biosynthetic protein FliP
lmo0677		similar to flagellar biosynthesis protein FliQ
lmo0678		similar to flagellar biosynthetic protein FliR
lmo0693	fliY	flagellar motor switch domain protein
lmo0785		similar to transcriptional regulator (NifA/NtrC family)
lmo0789		similar to conserved hypothetical proteins
lmo0790		similar to transcription regulator (EbsC from <i>Enterococcus faecalis</i>)
lmo0799		unknown
lmo0810		spermidine/putrescine ABC transporter, spermidine/putrescine-binding protein
lmo0811		carbonic anhydrase
lmo0834		membrane protein, putative
lmo0836		similar to <i>B. subtilis</i> YrkR protein
lmo0843		similar to <i>B. subtilis</i> protein YsdA
lmo0867		unknown
lmo0881		unknown
lmo0882		similar to <i>B. subtilis</i> YdbS protein
lmo0908		similar to membrane proteins
lmo0910		glycerol uptake facilitator protein
lmo0935		similar to <i>B. subtilis</i> CspR protein, rRNA methylase homolog
lmo0936		similar to Nitroflavin-reductase
lmo0937		unknown
lmo0943	fri	non-heme iron-binding ferritin
lmo0945		similar to C-terminal part of <i>B. subtilis</i> ComEC protein and to ComEA
lmo0950		unknown
lmo0957		glucosamine-6-phosphate isomerase
lmo0992		conserved hypothetical protein
lmo0993		cation transport protein
lmo1028		similar to <i>B. subtilis</i> YkzG protein
lmo1059		unknown
lmo1219		unknown
lmo1220		similar to unknown protein
lmo1221	pheS	phenylalanyl-tRNA synthetase alpha subunit
lmo1257		unknown
lmo1260	proB	gamma-glutamyl kinase
lmo1267	tig	trigger factor (prolyl isomerase)
lmo1333		similar to <i>B. subtilis</i> YqzC protein
lmo1334		similar to <i>B. subtilis</i> YqzD protein
lmo1337		similar to <i>B. subtilis</i> yqgP
lmo1366		conserved hypothetical protein
lmo1368	recN	DNA repair and genetic recombination
lmo1389		similar to sugar ABC transporter, ATP-binding protein
lmo1394		similar to 3-ketoacyl-acyl carrier protein reductase
lmo1405		similar to putative anti-terminator regulatory protein
lmo1406	pflB	pyruvate formate-lyase

lmo1493		similar to oligopeptidase
lmo1494		similar to 5-methylthioadenosine/S-adenosylhomocysteine nucleosidase
lmo1495		similar to unknown proteins
lmo1509		similar to exodeoxyribonuclease V
lmo1510		similar to unknown proteins
lmo1595		similar to unknown protein
lmo1603		aminopeptidase, putative
lmo1609		thioredoxin family protein
lmo1625		MW1697
lmo1683		similar to transcription regulators (Fur family), PerR in <i>B. subtilis</i>
lmo1685	gsaB	glutamate-1-semialdehyde-2,1-aminomutase 2
lmo1687		similar to hypothetical proteins
lmo1697		cation efflux family protein
lmo1703		RNA methyltransferase, TrmA family
lmo1705		deoxynucleoside kinase family protein
lmo1736		similar to unknown proteins
lmo1737		alcohol dehydrogenase, iron-dependent
lmo1740		conserved hypothetical protein
lmo1741		similar to two-component sensor histidine kinase
lmo1742	adeC	highly similar to adenine deaminases
lmo1743		unknown
lmo1762		bacteriochlorophyll synthase, 43 kDa subunit
lmo1781		unknown
lmo1849		manganese ABC transporter, ATP-binding protein
lmo1850		similar to transcriptional regulator (MarR family)
lmo1851		similar to carboxy-terminal processing proteinase
lmo1860		similar to peptidyl methionine sulfoxide reductases
lmo1861		conserved hypothetical protein
lmo1864		hemolysin III
lmo1865		similar to conserved hypothetical proteins
lmo1877		formate--tetrahydrofolate ligase
lmo1881		5'-3' exonuclease family protein
lmo1918		similar to unknown proteins
lmo1940		similar to asparaginase
lmo1973		similar to PTS system enzyme II A component
lmo1974		similar to transcription regulators, (GntR family)
lmo1980		unknown
lmo1992		similar to alpha-acetolactate decarboxylase
lmo2050		daunorubicin resistance protein
lmo2054		conserved hypothetical protein
lmo2055		similar to unknown proteins
lmo2056		similar to unknown proteins
lmo2057	ctaB	protoheme IX farnesyltransferase
lmo2058	ctaA	similar to heme O oxygenase
lmo2059		similar to potassium channel subunit
lmo2079		unknown
lmo2086		weakly similar to transcription regulators
lmo2105		similar to ferrous iron transport protein B
lmo2107		transcriptional regulator, DeoR family
lmo2148		similar to unknown proteins
lmo2157	sepA	sepA
lmo2187		unknown
lmo2203		N-acetylmuramoyl-L-alanine amidase, family 4
lmo2207		membrane protein, putative
lmo2208		similar to unknown protein

lmo2216		similar to histidine triad (HIT) protein
lmo2238		similar to transport system permease protein
lmo2239		unknown
lmo2240		similar to ABC transporter (ATP-binding protein)
lmo2242		similar to O6-methylguanine-DNA methyltransferase
lmo2243		similar to methylphosphotriester-DNA alkyltransferase and transcriptional regulator
lmo2244		similar to putative ribosomal large subunit pseudouridine synthase
lmo2246		similar to unknown proteins
lmo2264		similar to unknown proteins
lmo2362		similar to amino acid antiporter (acid resistance)
lmo2408		similar to repressor protein
lmo2419		similar to ABC transporter (ATP-binding protein)
lmo2430		iron compound ABC transporter, permease protein
lmo2433		similar to acetyltransferase
lmo2439		unknown
lmo2451		similar to preprotein translocase subunit SecG
lmo2452		similar to carboxylesterase
lmo2469		similar to amino acid transporter
lmo2470	inlP	similar to internalin proteins
lmo2471		similar to NADH oxidase
lmo2490		similar to B. subtilis CsbA protein
lmo2515		similar to B. subtilis two-component response regulator DegU
lmo2547		homoserine dehydrogenase
lmo2552	murZ	UDP-N-acetylglucosamine 1-carboxyvinyltransferase
lmo2567		conserved hypothetical protein
lmo2637		similar to spermidine N1-acetyltransferase
lmo2638		pyridine nucleotide-disulfide oxidoreductase family protein
lmo2657		deoxyguanosinetriphosphate triphosphohydrolase
lmo2705		conserved hypothetical protein
lmo2733		PTS system, fructose-specific, IIABC component
lmo2751		ABC transporter, ATP-binding/permease protein
lmo2766		phosphosugar-binding transcriptional regulator, RpiR family
lmo2842		transcriptional regulator, LacI family
lmo2849		quinol oxidase AA3, subunit I
lmo539		tagatose 1,6-diphosphate aldolase, putative
lmos10	LhrC-4	miscRNA
lmos27	rli33	miscRNA
lmos50	rli42	miscRNA

Table S1. Genes absent in liver vs BHI, placenta vs BHI, placenta vs liver.

<u>1 = Normal to minimal breakdown</u>	
Hypereosinophilic necrosis	Minimal. No areas of contiguous necrosis >0.2mm
Trophoblast giant cell viability	Few are pyknotic
Karyorrhectic debris	Minimal
<u>2 = Minimal breakdown</u>	
Hypereosinophilic necrosis	Focal, some necrotic areas >0.2 mm but <1 mm in greatest dimension
Trophoblast giant cell viability	Some are pyknotic
Karyorrhectic debris	Minimal
<u>3 = Moderate breakdown</u>	
Hypereosinophilic necrosis	Larger (>1mm but <2mm in length) areas of complete breakdown
Trophoblast giant cell viability	Majority of giant cells appear as dead eosinophilic "ghosts"
Karyorrhectic debris	Moderate
<u>4 = Severe breakdown</u>	
Hypereosinophilic necrosis	Most tissue involved, contiguous zones measure >2mm in length
Trophoblast giant cell viability	Only rare, barely discernible dead "ghost" cells seen
Karyorrhectic debris	Moderate

Table S2. Histopathology scoring system for decidual necrosis. Summary of the criterion utilized by pathologist for blinded-scoring of implantation site pathology in placentas from infected guinea pigs (results in Fig. 4).